

Serial No. 10/789,956
Docket No. SHE0081.00

AMENDMENTS

RECEIVED
CENTRAL FAX CENTER
AUG 23 2006

In the Claims:

Please amend claims 1 and 26-30 as indicated below. Currently amended claims are presented with markings to indicate the changes made, wherein a ~~strike through~~ is used to designate deletions and underlining is used to designate additions.

1. (Currently Amended) A conjugate comprising one, two or three water-soluble polymers covalently attached to a Factor VIII moiety, wherein each water-soluble polymer has a nominal average molecular weight in the range of from 6,000 Daltons to 150,000 Daltons and further wherein the conjugate is a 1-mer, 2-mer or 3-mer.

2. (Previously Presented) The conjugate of claim 1, wherein each water-soluble polymer in each conjugate is selected from the group consisting of a poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, and poly(acryloylmorpholine).

3. (Previously Presented) The conjugate of claim 2, wherein each water-soluble polymer is a poly(alkylene oxide).

4. (Previously Presented) The conjugate of claim 3, wherein each poly(alkylenc oxide) is a poly(ethylene glycol).

5. (Previously Presented) The conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with an end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.

6. (Previously Presented) The conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with methoxy.

Serial No. 10/789,956
Docket No. SHE0081.00

7. (Previously Presented) The conjugate of claim 4, wherein the poly(ethylene glycol) is terminally capped with hydroxy.

8. (Previously Presented) The conjugate of claim 4, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from 6,000 Daltons to 100,000 Daltons.

9. (Previously Presented) The conjugate of claim 8, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from 10,000 Daltons to 85,000 Daltons.

10. (Previously Presented) The conjugate of claim 9, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from 20,000 Daltons to 85,000 Daltons.

11. (Previously Presented) The conjugate of claim 10, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from 53,000 Daltons to 75,000 Daltons.

12. (Previously Presented) The conjugate of claim 3, wherein each water-soluble polymer is linear.

13. (Previously Presented) The conjugate of claim 3, wherein each water-soluble polymer is branched.

14. (Previously Presented) The conjugate of claim 3, wherein the Factor VIII moiety is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF, and B-domain deleted Factor VIII.

15. (Previously Presented) The conjugate of claim 14, wherein the Factor VIII moiety is selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, and Factor VIII:vWF.

16. (Previously Presented) The conjugate of claim 14, wherein the Factor VIII moiety is B-domain deleted Factor VIII.

Serial No. 10/789,956
Docket No. SHE0081.00

17. (Previously Presented) The conjugate of claim 3, wherein the Factor VIII moiety is recombinantly derived.

18. (Previously Presented) The conjugate of claim 3, wherein the Factor VIII moiety is blood-derived.

19. (Previously Presented) The composition of claim 62, wherein the composition is substantially free of albumin.

20. (Previously Presented) The composition of claim 62, wherein the composition is substantially free of proteins that do not have Factor VIII activity.

21. (Previously Presented) The composition of claim 62, wherein the composition is substantially free of noncovalently attached water-soluble polymers.

22. (Previously Presented) The composition of claim 62, wherein at least one water-soluble polymer is covalently attached to a site in the active form of the moiety having Factor VIII activity.

23. (Previously Presented) The composition of claim 62, in lyophilized form.

24. (Previously Presented) The composition of claim 62, in the form of a liquid.

25. (Previously Presented) The composition of claim 62, further comprising a pharmaceutically acceptable excipient.

26. (Currently Amended) The conjugate of claim 1, wherein ~~each conjugate comprises~~ the one, two or three water-soluble polymers are covalently attached by an amide linkage.

Serial No. 10/789,956
Docket No. SHE0081.00

27. (Currently Amended) The conjugate of claim 1, wherein ~~each conjugate comprises~~
the one, two or three water-soluble polymers are covalently attached by a secondary amine
linkage.

28. (Currently Amended) The conjugate of claim 1, wherein ~~each conjugate comprises~~
the one, two or three water-soluble polymers are covalently attached by a carbamate linkage.

29. (Currently Amended) The conjugate of claim 1, wherein ~~each conjugate comprises~~
the one, two or three water-soluble polymers are covalently attached by a thioether linkage.

30. (Currently Amended) The conjugate of claim 1, wherein ~~each conjugate comprises~~
the one, two or three water-soluble polymers are covalently attached by a disulfide linkage.

31. (Withdrawn) A composition comprising a plurality of monoPEGylated Factor VIII
moiety conjugates.

32. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor
VIII moiety conjugate comprises one poly(ethylene glycol) terminally capped with an
end-capping moiety selected from the group consisting hydroxy, alkoxy, substituted alkoxy,
alkenoxy, substituted alkenoxy, alkynoxy, substituted alkynoxy, aryloxy and substituted aryloxy.

33. (Withdrawn) The composition of claim 31, wherein the poly(ethylene glycol) is
terminally capped with methoxy.

34. (Withdrawn) The composition of claim 31, wherein the poly(ethylene glycol) is
terminally capped with hydroxy.

35. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor
VIII moiety conjugate comprises a poly(ethylen glycol) having a nominal average molecular
weight in the range of greater than 5,000 Daltons to about 150,000 Daltons.

Serial No. 10/789,956
Docket No. SHE0081.00

36. (Withdrawn) The composition of claim 35, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 6,000 Daltons to about 100,000 Daltons.

37. (Withdrawn) The composition of claim 36, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 10,000 Daltons to about 85,000 Daltons.

38. (Withdrawn) The composition of claim 37, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 20,000 Daltons to about 85,000 Daltons.

39. (Withdrawn) The composition of claim 38, wherein the poly(ethylene glycol) has a nominal average molecular weight in the range of from about 53,000 Daltons to about 75,000 Daltons.

40. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a linear poly(ethylene glycol).

41. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety comprises a branched poly(ethylene glycol).

42. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, Factor VIII:vWF, B-domain deleted Factor VIII, and biologically active fragments, deletion variants, substitution variants or addition variants of any of the foregoing.

43. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety selected from the group consisting of Factor VIII, Factor VIIIa, Factor VIII:C, and Factor VIII:vWF.

Serial No. 10/789,956
Docket No. SHE0081.00

44. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises B-domain deleted Factor VIII.

45. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety that is recombinantly derived.

46. (Withdrawn) The composition of claim 31, wherein each monoPEGylated Factor VIII moiety conjugate comprises a Factor VIII moiety that is blood-derived.

47. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of albumin.

48. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of proteins that do not have Factor VIII activity.

49. (Withdrawn) The composition of claim 31, wherein the composition is substantially free of noncovalently attached water-soluble polymers.

50. (Withdrawn) The composition of claim 31, in lyophilized form.

51. (Withdrawn) The composition of claim 31, in the form of a liquid.

52. (Withdrawn) The composition of claim 31, further comprising a pharmaceutically acceptable excipient.

53. (Withdrawn) The composition of claim 31, wherein each conjugate comprises an amide linkage.

54. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a secondary amine linkage.

Serial No. 10/789,956
Docket No. SHE0081.00

55. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a carbamate linkage.

56. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a thioether linkage.

57. (Withdrawn) The composition of claim 31, wherein each conjugate comprises a disulfide linkage.

58. (Withdrawn) A method for making a conjugate comprising contacting, under conjugation conditions, a Factor VIII moiety with a polymeric reagent.

59. (Withdrawn) A method for treating a patient in need of Factor VIII therapy, comprising the step of administering to the patient the composition of claim 1 or claim 31, wherein the composition contains a therapeutically effective amount the conjugates.

60. (Withdrawn) The method of claim 59, wherein the patient is suffering from hemophilia A.

61. (Withdrawn) The method of claim 59, wherein the patient is administered the composition within two days prior to undergoing surgery.

62. (Previously Presented) A composition comprising the conjugate of claim 3.

(This space intentionally left blank.)